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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,727	02/13/2002	John T. Groves	IB-1695	2093
8076	7590	11/05/2007		
LAWRENCE BERKELEY NATIONAL LABORATORY ONE CYCLOTRON ROAD, MAIL STOP 90B UNIVERSITY OF CALIFORNIA BERKELEY, CA 94720			EXAMINER SHIBUYA, MARK LANCE	
			ART UNIT 1639	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/076,727	Applicant(s) GROVES ET AL.	
	Examiner Mark L. Shibuya, Ph.D.	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 August 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7-20, 25 and 26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7-20, 25 and 26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Application 10076727, (20020160505 A1): Claims 7-20, 25 and 26 are pending and examined.

Priority

2. This application, 10/076,727, filed 2/13/2002, claims benefit of 60/269,625, filed 2/16/2001, and claims benefit of 60/296,952, filed 6/8/2001.

Withdrawn Claim Objections/Rejections

3. The following claim rejections/objections are withdrawn in view of applicant's arguments and amendments to the claims:
4. Claims 7, 8, and 14 are objected to because of the following informalities: The claims state: "a.", "b." and "c.". However, it is recommended practice to have only a final period in a claim. Appropriate correction is encouraged.
5. Claims 7-20, 25 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is for new matter. But

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see, the below new rejection under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

6. Claims 7-20, 25 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for stating the term "natural interaction" in claims 7 and 8.

New Claim Rejections - 35 USC § 112, First Paragraph

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 7-20, 25 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification as filed does not appear to provide support for methods comprising cell interaction that is a "functional cell-cell interaction", as in independent claims 7, 8 and 14. It is noted that the membranes in corrals are not cells.

The specification as filed does not appear to provide support for methods comprising "lipid bilayer membranes which *mimic* an artificial cell surface" (emphasis added), as in independent claim 14. Applicant must point, with particularity, as to where specific support for this limitation is to be found in the specification as filed.

Applicant states that although the specification does not provide literal, *in haec verba* support for the new claim limitations of cell interactions that are "a functional cell-cell interaction", support for the limitation may be found variously throughout the specification as filed, e.g., pp. 5-7 and 9 of the instant specification. Applicant points to Exhibit A, entered 2/3/2006, which is a publication by the first named inventor John (Jay) T. Groves, Sci STKE, 2005, Sep 13; 2005 (301):pe45, to show that the claimed methods are useful for observing and establishing functional cell-cell interaction studies.

Applicant's arguments, entered 8/10/2007, have been fully considered but they are not persuasive. The genus of functional cell-cell interactions include various species, including occluding junctions, such as "tight" junctions and septate junctions; communicating junctions, such as gap junctions; intermediate junctions, such as chemical synapses; and desmosomes, (see Copenhaver et al., Bailey's Textbook of Histology, Seventeenth Edition, The Williams & Wilkins Company/Baltimore, 1978, at pp. 108-122, including the drawing at p. 109). However, the specification does not provide a sufficient number of species of cell interaction observable in the claimed method, to adequately represent the genus of functional cell-cell interactions.

The examiner respectfully notes that in Exhibit A, Groves at p. 2, right hand column, first full paragraph, states:

Cell-Cell Signaling

Direct signaling between cells may represent an even more diverse problem than that of cell-ECM interactions. In cell-cell signaling, both receptors and ligands can reside in cell membranes, allowing for complex and active feedback from both interacting cells. This feedback can occur at many levels, from increased or decreased protein expression on the cell surfaces to cytoskeleton-driven spatial rearrangements of the receptors and ligands themselves. Neuronal synapses are widely known examples of intercellular signaling junctions. There has been interest in developing synthetic interfaces between neurons and solid-state materials, such as semiconductor integrated electronics. Although there have been successes with electronic triggering and detection of neuronal action potentials (7), the prospect of forming a genuine neuronal synapse with a synthetic device remains distant. The crux of the problem is similar to that encountered in cell-ECM interactions: The necessary signaling ligands must be displayed within an appropriate context to direct the cell into the desired mode of behavior.

Exhibit A at p. 2. Thus Groves discloses the unpredictability in making any species of the genus of functional cell-cell interactions.

Furthermore, it is noted that applicant points to the specification at pp. 5-7, for lymphocyte-endothelial interactions, wherein endothelial cell membranes are held in corrals. The examiner respectfully submits that this example is does not involve the use of dopants, and so is not relevant to and does not constitute support for the claims as amended

New Claim Rejections - 35 USC § 112, Second Paragraph

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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10. Claims 14-20, 25 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claim 14 states the new language "which *mimic* an artificial surface", (emphasis added), which renders the claims indefinite. As the lipid bilayer membranes are contained in corrals, it would appear that the said corralled membranes are artificial surface, themselves, and not merely mimicking an artificial surface. Thus one of skill in the art would not be reasonably apprised of the metes and bounds of the claimed invention.

Maintained Claim Rejections - 35 USC § 102

11. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

12. Claims 7, 8, 10, 11, and 14-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Dori et al., Biomedical Materials Research, (Sept. 7, 1999), p. 75-81, (IDS entered 5/26/2005).

This rejection is maintained for the reasons of record, as set forth in the previous Office action. This rejection is necessitated by applicant's amendments to the claims.

The claims are drawn to methods for screening living cell adhesion on a solid substrate comprising:

a) contacting a living cell with a micro-array comprising a substrate comprising an array of adjacent membrane corrals, wherein the corrals contain lipid bilayer membranes above an aqueous layer, wherein said lipid bilayer membranes are doped with one or more dopants to form a doped lipid bilayer membrane, said dopants selected from the group consisting of charged lipids and membrane proteins; and

b) observing cell interaction and adhesion to the doped lipid bilayer membranes after a time period of at least one hour, whereby the dopants direct cell interaction and adhesion, and wherein the cell interaction is a functional cell-cell interaction.

Dori et al., Ligand accessibility as means to control cell response to bioactive bilayer membranes, *Journal of Biomedical Materials Research*, 2000.50(1):p. 75-81, (IDS entered 5/26/2005), teaches cells adhesion to lipid bilayer membranes created by Langmuir-Blodgett deposition of either a pure poly(ethylene glycol) lipid having head groups of various lengths or binary mixtures of a poly(ethylene glycol) lipid and a novel collagen-like peptide amphiphile, reading on a membrane protein, on hydrophobic mica surface. Said bilayers on mica supports are then placed in a plurality of submerged glass vials, which read on microarrays. Dori, at p. 76 teaches micropatterned surfaces, which read on microarrays. Dori et al., teaches cell adhesion to a lipid bilayer membrane (see, e.g., Dori et al., throughout the publication and abstract, and especially Figures 4 and 5).

Response to Arguments

Applicant argues that Dori et al. does not teach the specific limitation that the dopants direct cell adhesion. Applicant contrasts the reference of Dori et al. to the

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instant invention by stating that the claimed method uses doping to direct or promote cell adhesion as opposed to making to prevent cell adhesion. Applicant argues that the claimed method comprises membranes that are freely accessible and mimic a cell's natural surface, unlike the membrane surfaces in Dori et al., which do not mimic natural lipid bilayers and require PEG lipids and peptide ligands bonded to the lipid head groups to control cell response

Applicant's arguments, entered 8/10/2007, have been fully considered but they are not persuasive. The instant claims state the limitations that dopants are selected from the group consisting of charged lipids and membrane proteins. Thus the membrane proteins are dopants. Applicant's reply, at p. 9, note that Dori et al. discloses that cells adhere and spread on mixtures of the peptide amphiphile with PEG lipids.

The examiner respectfully submits that applicant's arguments that Dori et al., does not teach methods for promoting adhesion of cells but rather methods of masking to prevent cell adhesion is too narrow a reading. Dori et al., in the title and in the first sentence, refer to controlling cell response bioactive membranes. Dori et al., at pp. 26-27, report the creation of three types of surfaces: surfaces that promoted both cell adhesion and spreading, surfaces that promoted cell adhesion but not cell spreading; and surfaces that did not promote cell adhesion or spreading. The examiner respectfully submits that the methods of controlling cell interaction, as taught by Dori et al., involve controlling the degree and specificity of cell adhesion, and not solely the prevention of cell adhesion.

Conclusion

13. Claims 7-20, 25 and 26 are rejected. Claims 7, 8, and 14 are objected to.

14. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Groves et al., Control of Cell Adhesion and Growth with Micropatterned Supported Lipid Membranes, Langmuir 2001, 17, 5129-5133.

Groves et al., Supported planar bilayers in studies on immune cell adhesion and communication, J. Immunol. Methods 278 (2003) 19-32.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Shibuya, whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Doug Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Mark L. Shibuya, Ph.D.
Primary Examiner
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